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description

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For two-letter codes and other abbreviations, refer to the "Guid-
ance Notes on Codes and Abbreviations" appearing at the begin-
ning of each regular issue of the PCT Gazette.

(54) Title: A BACTERIAL TWO-HYBRID SYSTEM FOR PROTEIN INTERACTION SCREENING

(57) Abstract: Two bacterial strains deficient in endogenous adenylate cyclase activity are provided. The strains, designated BTH101 and DHM1, are useful in a signal amplification system comprising a bacterial multi-hybrid system, and more preferably a two-hybrid system, of at least two chimeric polypeptides containing a first chimeric polypeptide corresponding to a first fragment of an enzyme and a second chimeric polypeptide corresponding to a second fragment of an enzyme or a modulating substance capable of activating said enzyme as described in published PCT application WO 99/28746. The signal amplification system is useful in a method of selecting a molecule of interest, which is capable of binding to target ligand, wherein the interaction between the molecule of interest and the target ligand is detected with the signal amplification system, and the kit therefor, as described in WO 99/28746. The strains are also useful in the method of screening for a substance capable of stimulating or inhibiting the interaction between a target ligand and a molecule of interest, and the kit therefor, as described in WO 99/28746.

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INTERNATIONAL SEARCH REPORT

International Application No

PCT/IB 01/00773

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 G01N33/542 C12N15/00 C12Q1/68 C12N5/00 G01N33/50
C12Q1/02 C12Q1/527

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 G01N C12Q

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data, PAJ, MEDLINE, BIOSIS

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 99 28746 A (LADANT DANIEL ;ULLMANN AGNES (FR); KARIMOVA GOUZEL (FR); PASTEUR I) 10 June 1999 (1999-06-10) cited in the application the whole document	10,11
X	KARIMOVA ET AL: "A bacterial two-hybrid system based on a reconstituted signal transduction pathway" PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF USA, NATIONAL ACADEMY OF SCIENCE. WASHINGTON, US, vol. 95, May 1998 (1998-05), pages 5752-5756, XP002100623 ISSN: 0027-8424 cited in the application the whole document	10,11

☐ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

* Special categories of cited documents:

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* earlier document but published on or after the international filing date
- *L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- *O* document referring to an oral disclosure, use, exhibition or other means
- *P* document published prior to the international filing date but later than the priority date claimed

- *T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- *X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- *Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- *G* document member of the same patent family

Date of the actual completion of the international search

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04/09/2002

Name and mailing address of the ISA

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Gundlach, B

INTERNATIONAL SEARCH REPORT

International application No.
PCT/IB 01/00773

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☒ Claims Nos.: 45, 46
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
see FURTHER INFORMATION sheet PCT/ISA/210
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Claims Nos.: 45,46

Present claims 45 and 46 relate to compounds (molecule, substance) defined by reference to a desirable characteristic or property, namely being identifiable by the screening methods of claims 13-25 or 29-43 resp.

The claims cover all compounds having this characteristic or property, whereas the application provides support within the meaning of Article 6 PCT and/or disclosure within the meaning of Article 5 PCT for no such compounds. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible. Independent of the above reasoning, the claims also lack clarity (Article 6 PCT). An attempt is made to define the compound by reference to a result to be achieved. Again, this lack of clarity in the present case is such as to render a meaningful search over the whole of the claimed scope impossible. Consequently, the search has been carried out for those parts of the claims which appear to be clear, supported and disclosed, namely those parts relating to the screening methods per se (claims 13-25 and 29-43).

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/IB 01/00773

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
WO 9928746	A	10-06-1999	US 6333154 B1	25-12-2001
			CA 2312379 A1	10-06-1999
			EP 1036323 A1	20-09-2000
			WO 9928746 A1	10-06-1999
			JP 2001525187 T	11-12-2001
			US 2002106783 A1	08-08-2002
